



# Not just minor resections: robotic approach for cystic echinococcosis of the liver

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## Abstract

**Introduction** Human echinococcosis is among the 17 neglected tropical diseases recognized by the World Health Organization. It is responsible for over \$3 billion of health costs every year being endemic in large areas worldwide, and liver is affected in 70% of the cases. Surgery associated to medical treatment is the gold standard and robotic approach may be a valuable tool to achieve safe, parenchyma sparing resections.

**Methods** We retrospectively analyzed the outcomes of patients that underwent robotic radical surgical treatment for hydatid liver disease, from prospectively maintained databases of three Italian centers.

**Results** 15 patients were included in this study, median age 51 years (24–76). 1 right hepatectomy, 2 left lateral sectionectomies, 5 segmentectomies (including 1 caudatectomy), 3 wedge resections and 5 cyst-pericystectomies were performed. Median estimated blood loss was of 100 ml (50–550 ml), and median operative time including docking was 210 min (95–590 min), with no need for conversion to open. Median hospital stay was 4 days, with only one readmission for fever. Only one patient experienced recurrence in a different liver segment.

**Conclusions** In our experience, robotic approach for cystic echinococcosis of the liver proved to be a safe and effective strategy also in the so-called “difficult segments”, with short post-operative stay and quick return to daily activities, along with the absence of surgical site recurrences. To the best of our knowledge, this is the largest report of robotic approach to hydatid liver disease.

**Keywords** Robotic liver resection · Robotic surgery · Hydatid disease · Da Vinci · Parenchyma sparing · Albendazole

## Introduction

Human echinococcosis is among the 17 neglected tropical diseases recognized by the World Health Organization (WHO) [1, 2]. It is responsible for over \$3 billion of health costs every year and is considered endemic in large areas worldwide. It is a zoonosis caused by larval forms of *Echinococcus* tapeworms found in the small intestine of carnivores. Among the recognized species, two are of medical importance—*E. granulosus* and *E. multilocularis*—causing cystic echinococcosis (CE) and alveolar echinococcosis in humans, respectively.

CE has a worldwide distribution and a highly variable human disease burden in the different endemic areas depending upon human behavioral risk factors, the diversity and ecology of animal host assemblages and the genetic diversity within *Echinococcus* species [3].

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In Europe, *E. granulosus* is present in most countries with the exception of Ireland, Iceland, and Denmark [3, 4]. The most endemic areas have been documented to be the Mediterranean regions where annual incidence rates for human cystic echinococcosis are 4–8 per 100,000 persons and parts of Eastern Mediterranean countries such as Bulgaria [5]. Liver is affected in 70% of the cases, and rupture of the cyst may result in anaphylaxis. In 1995, the WHO-IWGE developed a standardized classification that allows to stratify the cysts into three relevant groups: active (CE1 and 2), transitional (CE3) and inactive (CE4 and 5) [6]. CE3 transitional cysts may be differentiated into CE3a (with detached endocyst) and CE3b (predominantly solid with daughter vesicles). CE1 and CE3a are early stages and CE4 and CE5 late stages.

WHO-IWGE consider four options for treating CE: drugs, percutaneous methods, surgery and “watch and wait” [7]. The decision on which strategy should be adopted is based on cyst stage and localization, as well as center-specific resources and training. Cyst stages CE 4 and 5 can remain untreated with a “watch and wait” strategy. Although percutaneous methods have been reported with good results [7, 8], cysto-biliary fistulas need to be reliably excluded to prevent irreversible complications.

The cure rate for liver hydatid cysts treated with albendazole alone is below 60%. Only trials that included three months of albendazole treatment and surgery have cure rates > 90% [9–11]. Surgery associated with medical treatment is the gold standard in case of large CE2-CE3b cysts with multiple daughter vesicles, single liver cysts at risk of rupture, infected cysts, cysts communicating with the biliary tree and cysts exerting pressure on adjacent vital organs [7], and robotic approach may be a valuable tool to achieve safe, parenchyma sparing resections [12]. Therefore, we decided to collect data among three Italian centers with experience of robotic liver surgery to explore the results after robotic approach for cystic echinococcosis.

## Methods

### Data extraction and patient selection

We retrospectively analyzed the prospectively maintained databases from three Italian centers, University of Modena and Reggio Emilia, University of Pisa and Careggi University Hospital of Florence. Indication to surgical resection in our centers is always discussed in a multidisciplinary meeting involving surgeons, radiologists, hepatologists and oncologists, as previously described<sup>13</sup>. For hydatid disease, the treatment strategy is always planned with infectious disease physicians. All procedures were approved by the

institution’s supervisory committee, and patients agreed to use anonymous data for research purposes.

As previously described [13] both Child A and Child B patients and non-cirrhotic liver diseases are eligible for robotic resection. Selection criteria include esophageal varices ≤ grade 1, platelet count ≥ 50 × 10<sup>9</sup>/L and American Society of Anesthesiologists (ASA) Score ≤ 3. As later discussed, ultrasound scan (US) of the abdomen, triphasic computed tomography (CT) scans, and contrast-enhanced magnetic resonance (MR) imaging are part of the staging work-up of liver echinococcosis to plan the surgical strategy. ASA physical score more than three, heart failure, respiratory insufficiency and general contraindication to pneumoperitoneum were assessed as exclusion criteria from minimally invasive liver surgery (MILS).

A perioperative prophylaxis with albendazole is routinely prescribed with the following schedule: 1 cycle prior to surgery and 3 cycles postoperatively. It is deemed necessary to reduce the risk of secondary echinococcosis [14].

An informed consent was signed by each patient at least the day before surgery, including the authorization to keep audio-visual material of the surgical procedure and the perioperative and follow-up data in our Institutional prospectively maintained database. After surgery, all patients were followed at both surgical and infectious disease outpatient clinic at 3- or 6-month intervals. Follow-up examinations included clinical examination, liver function tests and imaging according to the multidisciplinary consensus.

### Surgical technique

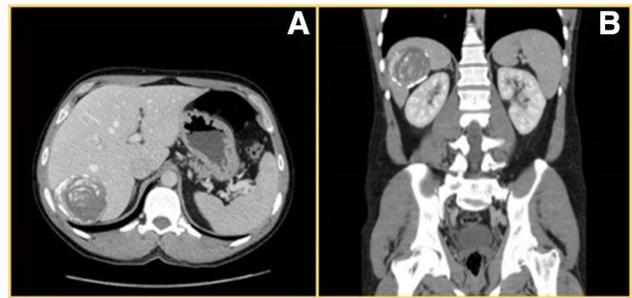
Robotic procedures were performed using the da Vinci Si or Xi Surgical System<sup>®</sup> (Intuitive Surgical Inc., Milford, CT, USA). Usually, the patient is in supine 15°–20° anti-Trendelenburg position and slightly rotated to the left to get access to right and posterior segments, however, a complete left decubitus is also an option. The pneumoperitoneum is induced with the Verres needle technique, from the left upper abdominal quadrant (Palmer’s point). Constant endoabdominal pressure is kept with the use of the automated insufflator AirSeal<sup>®</sup> (Surgiquest, Milford, CT, USA). The AirSeal trocar is used by the assistant to help with retraction or apply clips as needed by the surgeon at the robotic console.

The position of the first trocar for the scope is generally at the cross between right mid-clavicular line and transverse umbilical line. Exploratory laparoscopy is always performed to place three 8 mm robotic trocars before docking the patient chart of the robot. Notably, the set-up of the trocars may vary according to lesion localization and patient conformation. Parenchymal transection is performed with a combination of monopolar and bipolar energy and with the use of daVinci Harmonic ACE<sup>™</sup> (Ethicon, Somerville, NJ,

USA) for deeper layers, or PK gyrus (Olympus, Japan). The intraoperative ultrasound with TilePro™ function is always performed to define the transection plane. Cystopericystectomy is usually conducted with the use of bipolar and monopolar energy through the cleavage plane that is usually present between the smooth surface of the cyst and liver parenchyma. After the sample is extracted, hemostasis and biliostasis are perfected with fibrin glue and a JP drain tube is usually left in place.

## Radiological work-up

US is the first choice for radiological screening and is also useful in monitoring the effectiveness of medical therapy. The US appearance of the hydatid cyst may vary from simple to complex cyst with multi-vesicular, solid components, variable echogenic components and calcifications depending on the stage of evolution and maturity [15, 16]. As depicted in Fig. 1, US (A) shows a complex cyst in the VII segment of the liver, with sharp margins with probable wall calcifications and inhomogeneous content due to the presence of multi-folded linear echogenic formations. The CT scan (B, C) confirms the lesions, successively resected by surgery (D). CT is, in fact, the method of choice for the preoperative study of hydatid cyst, as it is able to evaluate the typical imaging findings, to examine its location, the relationships with the main vascular liver structures, any complications such as superinfection and possible biliary, vascular or extrahepatic extensions [15, 16]. Moreover, CT allows an adequate assessment of surgical resectability. CT imaging typically shows a round lesion with water attenuation density, surrounded by calcific ring (Fig. 2a, b), containing laminated—linear areas of increased attenuation. Usually, the presence of daughter cysts is displayed as round structures located peripherally within the mother cyst, that usually contain fluid with a lower attenuation than that of fluid of the mother cyst (Fig. 3a–c). The use of the CT contrast medium allows to visualize the peripheral enhancement of the cyst (pericyst) and to evaluate the anatomical relationships with the main vascular hepatic structures critical to a correct surgical planning [15, 16] (Fig. 4). Magnetic



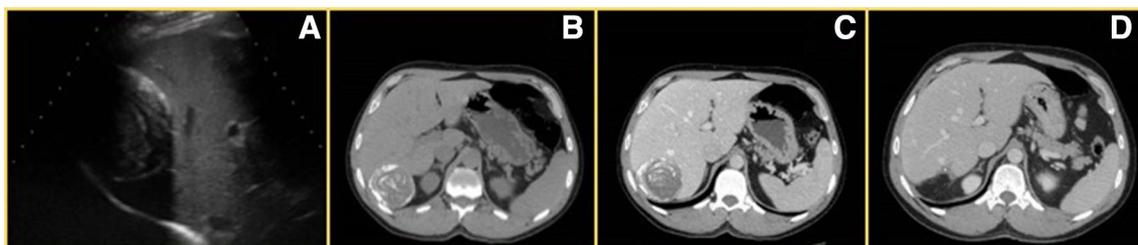
**Fig. 2** CT typical features of hydatid cyst: round lesion with water attenuation density, surrounded by calcific ring (a, b), containing laminated—linear areas of increased attenuation

resonance (MR) is the best imaging method to demonstrate a cystic component. The MR allows to confirm the CT hypothesis of cystic lesion and to visualize the lesion in different planes. The hydatid cyst may show variable sign intensities on T1 and T2 weighted images, according to the different components inside the lesion. A low-signal-intensity rim on T2 sequences corresponding to pericyst represents the characteristic sign of hydatid disease (Fig. 5a, b). After gadolinium contrast agent injection, the pericyst may show slight enhancement (Fig. 5c, d). At DW imaging the hydatid cysts are hyperintense at high *b* factor, different to simple cyst, and the apparent diffusion coefficient (Fig. 6a, c, d) is low due to difference in cyst components (Fig. 6e, f).

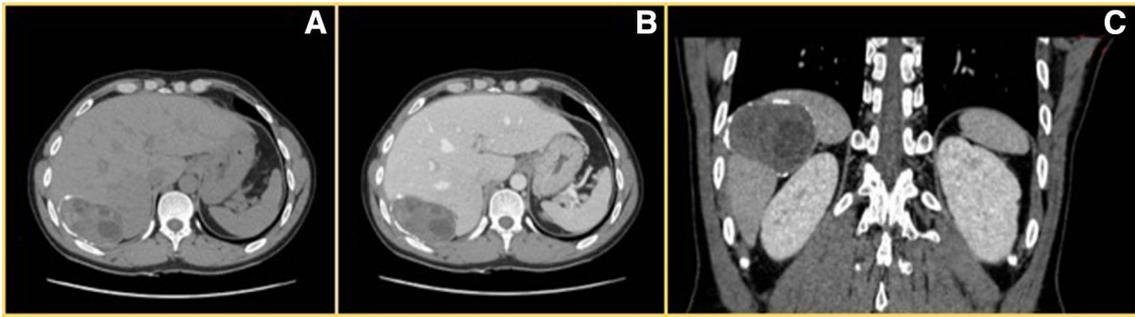
## Results

### Patients' characteristics

Fifteen patients for a total of sixteen cysts were finally included in this study and their general features are reported in Table 1. The cohort was relatively young and healthy. Male to female ratio was 8:7, mean age was 51 years (range 24–76). Mean BMI in was 23.05 (range 21–29), and there were no relevant comorbidities or severe ASA status. 1 right hepatectomy, 2 left lateral sectionectomies, 5 segmentectomies (including 1 caudatectomy), 3 wedge resections



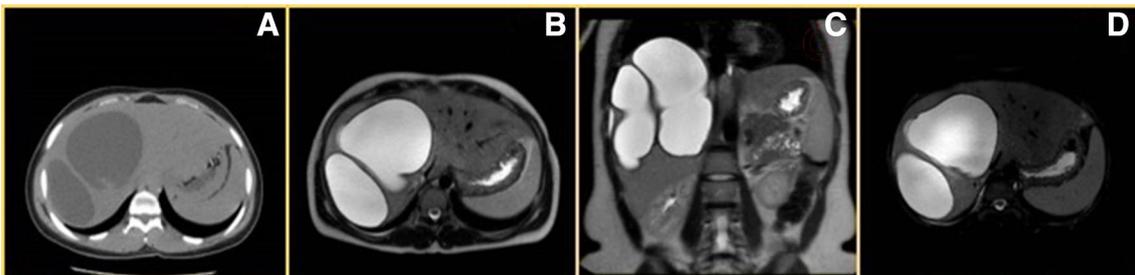
**Fig. 1** a Complex cyst in the VII segment of the liver, with sharp margins with probable wall calcifications and inhomogeneous content due to the presence of multi-folded linear echogenic formations. b, c CT scan confirms the lesions, successively resected by surgery (d)



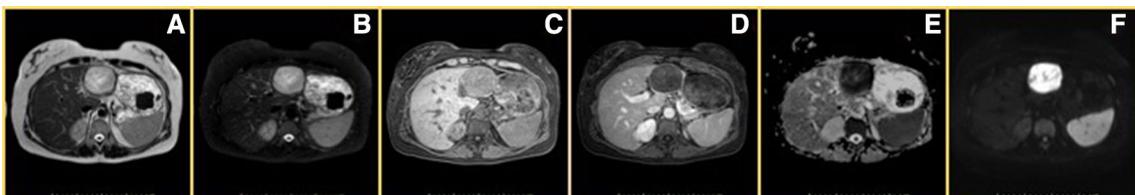
**Fig. 3** Presence of daughter cysts on CT imaging in a hydatid cyst of the VII segment: round structures located peripherally within the mother cyst, that usually contain fluid with a lower attenuation than that of fluid of the mother cyst (a–c)



**Fig. 4** Cyst of the caudate lobe: the contrast-enhanced CT scan allows to visualize the peripheral enhancement of the cyst (pericyst) and to evaluate the anatomical relationships with the main vascular hepatic structures critical to a correct surgical planning



**Fig. 5** Large hydatid cyst of the right lobe on MR. A low-signal-intensity rim on T2 sequences corresponding to pericyst represents the characteristic sign of hydatid disease (a, b). After gadolinium contrast agent injection the pericyst may show slight enhancement (c, d)



**Fig. 6** At DW imaging the hydatid cysts are hyperintense at high  $b$  factor, different to simple cyst, and the apparent diffusion coefficient (a, c, d) is low in rapport to difference in cyst components (e, f)

**Table 1** Clinical feature of patients included in the study

AGE (median, range)	51 (24–76)
Male/female	8/7
BMI (median, range)	23.05 (21–29)
ASA status	
ASA 1	5
ASA 2	8
ASA 3	2
WHO-IWGE classification of CE cysts	
CE1	1 (6.25%)
CE 2	5 (31.25%)
CE 3a	1 (6.25%)
CE 3b	3 (18.75%)
CE 4	3 (18.75%)
CE 5	3 (18.75%)
Comorbidities	
Hypertension	4
Diabetes mellitus	1
Depression	1

and 5 cyst-pericystectomies were performed. The sites of cyst-pericystectomies were segments 4, 5, 6 and 7, the latter occurred in two cases. All but one of the cases were at the first presentation of the disease. The mean follow-up in the patient cohort was 32.7 months (range 9.7–66.7).

50% of the cases had a formal indication to surgical resection after radiological staging (CE stage 2–3b). Among the others, three patients underwent surgical approach due to persistent abdominal pain, one patient presented with a large cyst of the caudate lobe which could not be approached with a percutaneous strategy and underwent isolated caudate lobe resection, and one patient presented with a diaphragmatic infiltration. Another patient underwent 2 years earlier a percutaneous aspiration of the cyst in another Hospital. At that time, she experienced spillage of the cyst and anaphylaxis. After complete recovery, she kept the cyst under control and finally came to the center of Modena due to persistent abdominal discomfort. She successfully underwent robotic left lateral sectionectomy without evidence of adhesions or satellite cysts.

### Intra and peri-operative data

Table 2 summarizes perioperative data. Median estimated blood loss was 100 ml (50–550 ml), and median operative time including docking was 210 min (95–590 min), with no need for conversion to open. One case required an en-block resection of the diaphragm along with segmentectomy of segment 6 due to suspect infiltration. The diaphragmatic defect was closed with a v-loc® (Medtronic, Minneapolis, MN, USA) running suture and a second layer with PDS

**Table 2** Intraoperative and perioperative data

Operative time (median min, range)	210 (95–550)
EBL (mean ml, range)	100 (50–550)
Conversion to open	0
Type of resection	
Right hepatectomy	1 (6.25%)
Left lateral sectionectomy	2 (12.5%)
Segmentectomy	5 (31.25%)
Wedge	3 (18.75%)
Cyst-pericystectomy	5 (31.25%)
Morbidity	
Clavien I–II	3
Clavien III–IV	1
Post-operative stay (median days, range)	4 (3–13)

interrupted sutures, and finally a chest tube was left in place. No abdominal nor chest recurrence was observed in this case after 1 year of follow-up. Notably, only one patient of the cohort (6.7%) experienced intraoperative spillage, due to misdiagnosis in the pre-operative work-up. She was scheduled for fenestration of a complicated hepatic cyst that intraoperatively resulted in a hydatid cyst. The revision of the images demonstrated a CE stage 3a cyst. Therefore, she started albendazole plus ivermectin after surgery. This patient eventually developed a recurrence in a different liver segment 1 year later and underwent a right hepatectomy with traditional open approach due to persistent abdominal pain and remittent fever. Median hospital stay was 4 days (3–13), with only one readmission for fever. No bile leaks nor development of intra-abdominal abscess occurred in this series. Only one patient required a re-intervention during the hospital stay due to small bowel perforation on p.o.d 2 that was treated with a laparoscopic over-sewn. It was probably an injury occurred while performing the Pfannestiel incision. In fact, the perforated small bowel loop was located in the lower quadrants and presented a small lesion without signs of ischemic injury of the bowel.

### Discussion

An accurate radiological work-up is crucial to drive the correct diagnosis and to provide a guide for surgeons to achieve a safe resection avoiding the rupture of the cyst. Surgical treatments for liver echinococcosis can be divided into two categories: radical approaches (cyst-pericystectomy, liver resection) and conservative approaches (unroofing or capitonnage) [17]. Contraindications to surgery in case of CE are (1) general patient-specific contraindications to surgery (2) inactive asymptomatic cysts (3) difficult to access cysts, and (4) very small cysts [7]. It has been reported that endoscopic

retrograde cholangiopancreatography (ERCP) can be a useful modality for therapeutic drainage when the cyst extends into the bile duct [18]. Recurrence rates after surgery for liver hydatid disease range from 2 to 25% in literature. The risk of recurrence is lower after radical procedures, and mostly due to either inadequate cyst removal or previously undetected cysts [17]. Also morbidity and mortality rates resulted to have lower incidence with radical procedures [14]. The decision whether to perform a radical or conservative approach for hydatid disease should be balanced on the risk of recurrence and, therefore, on the risk to be treated again for liver echinococcosis. A large multi-Institutional study reporting the outcomes of 232 patients treated for liver hydatid disease compared radical (73 patients) and conservative approaches (145 patients) [19]. The results highlighted that 6.9% of patients that received a less radical procedure were then re-operated due to recurrence within the first 3 years from the original procedure, while 5.5% required an additional procedure during the subsequent years. Eventually, they underwent a total pericystectomy, which was ultimately curative [19]. The study demonstrated also that conservative approaches are related to higher morbidity rates (24.13%,  $P=0.021$ ), and in particular biliary fistula (3.4% vs. 8%) and intra-abdominal abscess (3.4% vs. 6.9%) [19]. As depicted in Table 3, few data are reported in the literature about robotic approach to liver hydatid disease, and no large comparative analysis are available for open and minimally invasive procedures [20–26]. In a study from Iran published in 2015, 73 patients were prospectively assigned to either open or laparoscopic approach for uncomplicated hydatid liver cyst [27]. The technique in both groups consisted in cyst aspiration and unroofing, resulting in reduced operative time, postoperative pain, hospital stay, and time to return to work in the laparoscopic group as compared to the open group. No differences were reported about biliary leakage or fistula, that occurred in 33.3% of the entire population. However, besides the high incidence of biliary complications, this study presents a great bias, i.e. the exclusion from the cohort of patients that required a conversion from laparoscopic to open approach. From a technical perspective, the

precise dissection and stability of the robotic platform can reduce the risk of cystic rupture during cyst-pericystectomy. One of the most important advantages of the robotic platform as compared to other minimally invasive approaches is the TilePro™ function which consists in a simultaneous view at the console of up to three image sources, for example, the scope, the CT scan and the intraoperative ultrasound. With the intraoperative ultrasound, we precisely define size and position of the cyst and find the correct transection plane [13, 28, 29]. Moreover, the gentle tissue manipulation, the flexible instruments and the magnification of the image help the surgeon in dissecting around the cyst through the cleavage plan between the inner layer of the host's reaction towards the parasite and the cyst outer layer. In our experience, we were also able to conduct liver resections of difficult liver segments and in one case an en-block diaphragmatic resection. This represents another advantage of the robotic platform which provides high performances even in deep surgical fields and complex tasks. For example, the isolation of the cyst affecting the caudate lobe reported in this series required a cautious dissection of the hepatic artery and the control of short hepatic veins. Small bile ducts are also easily controlled with 5-0 PDS sutures to prevent post-operative leaks. Interestingly, no biliary fistula occurred in this robotic series, nor patients required re-operation due to echinococcosis recurrence when the disease was correctly diagnosed in the pre-operative setting. About one-third of the hydatid cysts in this cohort was treated with a meticulous and precise dissection of the pericystic layer. CE of the liver may require also major hepatic resections, like the case herein reported of a 28 years old male that received a right hepatectomy for an 8 cm mass of the right lobe (CE stage 3b). The patient was discharged from the hospital on post-operative day 3, in good general conditions and with prompt return to daily lives activities. This represent indeed one of the advantages that a minimally invasive approach to the liver may confer to patient rehabilitation, in particular in the setting of a relatively benign disease. No conversion to the open approach occurred in this cohort, confirming the agility of the robot to adapt to difficult intraoperative scenarios. The debate on the costs of robotic surgery is still open, however, the quality of papers analyzing this topic has been questioned [30]. Although we did not perform a formal cost-analysis, our results show a decrease of costs related to the management of complications, namely endoscopic procedures or re-intervention for biliary fistula or disease recurrence, and short in-hospital stay. Currently, it seems advisable to develop new minimally invasive frontiers for liver resections in centers with a solid background in hepatobiliary diseases management, with a multidisciplinary team to plan tailored therapeutic strategies, in order to find the best applications for the new technologies and to achieve an optimal allocation of the resources.

**Table 3** Literature review of robotic approach for liver hydatid disease

Author	Year	No of cases
Giulianotti et al. [20]	2011	2
Casciola et al. [21]	2011	2
Troisi et al. [22]	2013	4
Di Benedetto et al. [23]	2016	1
Quijano et al. [24]	2017	3
Zou et al. [25]	2017	1
Goja et al. [26]	2017	1

## Conclusions

In our experience, robotic approach for cystic echinococcosis of the liver proved to be a safe and effective strategy also in the so-called “difficult segments”, with short post-operative in-hospital stay, low incidence of liver-related post-operative complications, and quick return to daily activities, along with the absence of surgical site recurrences. To the best of our knowledge, this is the largest report of robotic approach to hydatid liver disease.

## Compliance with ethical standards

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

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